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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte ALBERTO L. MENDOZA

Appeal 2009-010875[1]
Application 09/082,112
Technology Center 1600

Before TONI R. SCHEINER, DEMETRA J. MILLS, and
LORA M. GREEN, *Administrative Patent Judges*.

MILLS, *Administrative Patent Judge*.

DECISION ON APPEAL[2]

This is an appeal under 35 U.S.C. § 134. The Examiner has rejected the claims for obviousness. We have jurisdiction under 35 U.S.C. § 6(b).

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[1] Note our prior Decision dated January 5, 2005.

[2] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, or for filing a request for rehearing, as recited in 37 C.F.R. § 41.52, begins to run from the "MAIL DATE" (paper delivery mode) or the "NOTIFICATION DATE" (electronic delivery mode) shown on the PTOL-90A cover letter attached to this decision.

STATEMENT OF CASE

The following claim is representative.

16. A method for treatment of an infection caused by *Pythium insidiosum* in human patients which comprises:

(a) providing a vaccine containing a mixture of (1) mixed intracellular proteins and (2) mixed extracellular proteins of *Pythium insidiosum* in a sterile aqueous solution, wherein the mixed intracellular proteins, which consist essentially of the intracellular proteins removed as a supernatant separated from disrupted cells of the *Pythium insidiosum* grown in a culture medium, and the mixed extracellular proteins, which consist essentially of proteins removed from the culture medium for growing the *Pythium insidiosum* the mixed intracellular proteins and the mixed extracellular proteins have been precipitated together with acetone, separated and then mixed with water and the mixture has been dialyzed to remove low molecular weight components less than 10,000 MW; and

(b) vaccinating human the patient with the vaccine .

Cited References

Mendoza et al., *Evaluation of two vaccines for the treatment of pythiosis insidiosi in horses*, 119 Mycopathologi. 89-95 (1992) ("92a").

Mendoza et al., *Immunoblot Analysis of the Humoral Immune Response to Pythium insidiosum in Horses with Pythiosis*, 30 Journal of Clinical Microbiology, 2980-2983 (1992) ("92b").

Mendoza et al. *Infections caused by the Oomycetous Pathogen*, 6 Journal Mycol. Med, 151-164 (1996) ("96").

Mendoza, *The Third NIAID Workshop in Medical Mycology Series*, Immunology in Medical Mycology, Series Abstracts, (1995) ("95").

Blanch et al. *Biochemical Engineering*, Marcel Dekker, (1996).

Amicon, *Catalog with Prices*, Membrane Filtration Chromatography, (1993)

Fisher, *Biotechnology Catalog*, Products for Life Science Research, (1995)

Grounds of Rejection

1. Claims 18, 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mendoza et al. (92a) in view of Mendoza et al. (92b), Mendoza, Amicon 1993 catalog, and Fisher 1995 catalog.

2. Claims 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mendoza et al. (92a), Mendoza et al. (92b), Mendoza (95), Amicon 1993 catalog, and Fisher 1995 catalog as applied to claims 18, 20-22 above, and further in view of Mendoza et al (96).

Discussion

ISSUE

The Examiner concludes that:

> it would have been *prima facie* obvious to a person of ordinary skill in the art at the time of invention to administer, to mammals, a pythiosis vaccine comprising a mixture of mixed intracellular proteins (especially including the three immunodominant proteins of Mendoza (92b)) and mixed extracellular proteins because Mendoza (95) teaches that a vaccine comprising a mixture of three immunodominant intracellular proteins and extracellular proteins was more successful in curing horses than either the CMV [cell-mass vaccine] or SCAV [Soluble Concentrated Antigen Vaccine] vaccines, and because

> Mendoza (92b) teaches that there are at least 20 reactive antigens found in the intracellular proteins of *Pythium isidiosum* that might be useful in immunotherapy.

(Ans. 6.)

Appellant contends that:

> [S]ince [the soluble intracellular protein composition of Medoza et al. (92b) includes numerous intracellular protein antigens as found in the cell-mass vaccine (CMV) of Mendoza et al. (92a), one skilled in the art would conclude that a horse would produce a prominent inflammatory response at the site of inoculation with the vaccine, as taught by Mendoza et al. (92a). Since these are undesirable properties in a vaccine, one of ordinary skill in the art, in view of Mendoza et al. (92a) and Mendoza et al. (92b), would not be motivated to create a vaccine containing all of the soluble intracellular proteins greater than 10,000 MW for treating Pythiosis in mammals. A person of ordinary skill in the art would not be motivated to add any additional proteins beyond the three prominent proteins (28-32 kD) of the vaccine of Mendoza (95) to avoid the prominent inflammatory response described by Mendoza et al. (92a).

(App. Br. 15.)

The issue is: Is there a sufficient reason or rationale to combine the cited references as suggested by the Examiner?

PRINCIPLES OF LAW

"[W]hen the question is whether a patent claiming the combination of elements of prior art is obvious" the relevant inquiry is "whether the improvement is more than the predictable use of prior art elements according to their established functions." *KSR Int'l Co. v. Teleflex Inc.*, 127 Ct. 1727, 1740 (2007).

FINDINGS OF FACT

1. Mendoza et al. (92a) teach subcutaneous administration of two vaccines for pythiosis, the Cell Mass Vaccine (CMV), and the Soluble Concentrated Antigen Vaccine (SCAV) to mammals. (abstract)

2. In Mendoza et al. (92a) the CMV consists of mixed intracellular antigens of *P. insidiosum* obtained by culturing *P. insidiosum* (ATCC 58643) in Sabouraud's dextrose broth. The cells were removed from the culture medium and disrupted by homogenization to provide the antigens for the vaccine (p. 90, col. 2).

3. In Mendoza et al. (92a) the SCAV consists of extracellular proteins obtained by culturing *P. insidiosum* (ATCC 58643) in Sabouraud's dextrose broth. The extracellular antigens were concentrated with a stir cell and precipitated with acetone (p. 91, col. 2 and p.92 col. 1).

4. Mendoza et al. (92a) teach that both vaccines were successful in curing cases of pythiosis in horses (p. 91, col. 2, paragraph 2). Mendoza et al. (92a) further teach that the etiological agent of pythiosis in horses, cattle, dogs, cats, and humans is Pythium isidiosum, and that nine strains isolated from humans, horses, and dogs with the disease were all the same species (p. 89, paragraph 1).

5. Mendoza et al. (92a) differs from the instant invention in that it does not teach that the intracellular proteins are separated from the disrupted cells in the CMV or the use of sonication to disrupt the cells. Mendoza et al. (92a) further does not teach the use of dialysis to remove components less than 10,000 MW or a vaccine that is a mixture of the intracellular and extracellular proteins. (Ans. 5.)

6. Mendoza et al. (92b) teach alternative methods to produce intracellular and extracellular protein pythiosis vaccines. (Ans. 5.)

7. In Mendoza et al. (92b) the composition containing the intracellular proteins was produced by culturing P. insidiosum, killing the cells with Merthiolate (thimersol), sonicating the cells to disrupt them and release intracellular proteins, then separated from the cell debris by centrifugation (p. 2981, col. 1, paragraph 1).

8. In Mendoza et al. (92b) an alternative method to produce a composition containing extracellular proteins is also taught. Cultures were killed with Merthiolate (thimersol), filtered to remove cells, and a stir cell with PM-10 membrane (Amicon) was used to concentrate the antigen (and remove low molecular weight components) (p. 2981, col. 1, paragraph 2).

9. Mendoza 92b also teach the important antigens found in the CMV vaccine and disclose that in addition to three immunodominant proteins (32K, 30K, and 28K) there are at least 20 antigens found in the intracellular proteins of Pythium isidiosum that are reactive in horse sera (p. 2981, col. 2, paragraph 3) and suggest that vaccines should include the three immunodominant proteins (p. 2982, col. 2, paragraph 3). Mendoza et al. (92b) also teach that five strains of Pythium isidiosum all had similar intracellular protein profiles.

10. Mendoza (95) teaches a vaccine that combined extracellular pythium antigens and the three immunodominant intracellular proteins of Mendoza (92b) and that said vaccine had an enhanced therapeutic effect on horses (see abstract). Mendoza (95) further teaches that hyphal antigens may contain products that are directly involved in the enhancement of the immunological response to vaccination (see abstract). (Ans. 5.)

11. The Amicon 1993 catalog teaches that a PM 10 membrane will retain molecules larger than 10,000 MW (p. 35). (Ans. 5.)

12. The Fisher 1995 catalog teaches dialysis membranes which will retain molecules larger than 10,000 MW (p. 56). (Ans. 6.)

13. The Examiner concludes that, as to claims 18, 20-22, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time of invention to administer, to mammals, a pythiosis vaccine comprising a mixture of mixed intracellular proteins (especially including the three immunodominant proteins of Mendoza (92b)) and mixed extracellular proteins because Mendoza (95) teaches that a vaccine comprising a mixture of three immunodominant intracellular proteins and extracellular proteins was more successful in curing horses than either the CMV or SCAV vaccines, and because Mendoza (92b) teaches that there are at least 20 reactive antigens found in the intracellular proteins of *Pythium isidiosum* that might be useful in immunotherapy. (Ans. 6.)

14. The Examiner concludes that it would also have been *prima facie* obvious to a person of ordinary skill in the art at the time of invention to use the method obtain the intracellular antigens by culturing *P. insidiosum,* killing the cells with Merthiolate (thimersol), sonicating the cells to disrupt them and release intracellular proteins, then separated from the cell debris by centrifugation because it would be easier to obtain the intracellular proteins this way, rather than using electrophoresis to obtain only the three immunodominant proteins. (Ans. 6.)

15. The Examiner concludes that the ordinary artisan would also have been motivated to use dialysis instead of a stir-cell with a PM 10 membrane because dialysis is significantly cheaper and provides for large batches.

Further, as taught by the Amicon and Fisher catalogs, the removal of small molecules of less than 10,000 MW by the PM10 membrane and the dialysis membrane is functionally equivalent. (Ans. 6.)

16. In Mendoza 92a, "Half of the horses vaccinated with CMV developed violent reactions with sterile abscesses. Horses with lesions between 1.5 or less months in age always developed a marked inflammatory reaction to both vaccines. (Mendoza 92a, page 91, paragraph bridging cols. 1 and 2.)

ANALYSIS

We preliminarily note that the claims have been amended since our earlier Decision in this case dated January 5, 2005.

Appellant contends that since the claimed vaccine includes numerous intracellular protein antigens as found in the cell-mass vaccine (CMV) of Mendoza et al. (92a), one skilled in the art would conclude that a horse would produce a prominent inflammatory response at the site of inoculation with the vaccine, as taught by Mendoza et al. (92a). Since these are undesirable properties in a vaccine, one of ordinary skill in the art, in view of Mendoza et al. (92a) and Mendoza et al. (92b), would not be motivated to create a vaccine containing all of the soluble intracellular proteins greater than 10,000 MW for treating Pythiosis in mammals. A person of ordinary skill in the art would not be motivated to add any additional proteins beyond the three prominent proteins (28-32 kD) of the vaccine of Mendoza (95) to avoid the prominent inflammatory response described by Mendoza et al. (92a).

We first interpret the claims before us. With respect to the intracellular components of the claimed vaccine, the claims require that the

mixed intracellular proteins consist essentially of the intracellular proteins removed as a supernatant separated from disrupted cells of the *Pythium insidiosum* grown in a culture medium. Thus, the intracellular proteins encompass multiple antigens found in the supernatant and are not limited to the three prominent antigens found in the CMV or intracellular portion as in Mendoza 92b and Mendoza 95.

We agree with Appellants that a person of ordinary skill in the art would not have been motivated to add any additional proteins beyond the three prominent proteins (28-32 kD) of the vaccine of Mendoza (92b and 95) to avoid the prominent inflammatory response described by Mendoza et al. (92a). (Br. 15.) The evidence of record before us would appear to reasonably show that antigens from the CMV cause violent inflammatory reactions and one of ordinary skill in the art would have tried to avoid such reactions, and thus would not have added multiple antigenic proteins to the CMV with inflammatory potential.

The rejection is reversed.

CONCLUSION OF LAW

The cited references do not support the Examiner's obviousness rejection. We reverse rejections 1 and 2.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

REVERSED

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